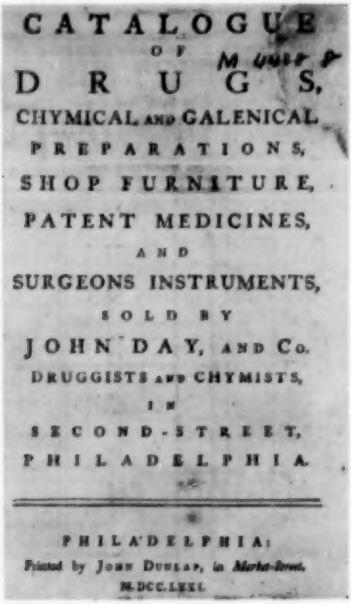
American Journal of Pharmacy

AND THE SCIENCES SUPPORTING PUBLIC HEALTH



CATALOGUE
OF
DRUGS,
CHYMICAL AND GALENICAL
PREPARATIONS,
SHOP FURNITURE,
PATENT MEDICINES,
AND
SURGEONS INSTRUMENTS,
SOLD BY
JOHN DAY, AND Co.
DRUGGISTS AND CHYMISTS,
IN
SECOND-STREET,
PHILADELPHIA.

PHILADELPHIA:
Printed by JOHN DUNLAP, in Market-Street.
M,DCC,LXXI.

JOHN DAY CATALOGUE OF DRUGS 1771

(See page 296)

Since 1825 *September 1955*

American Journal of Pharmacy

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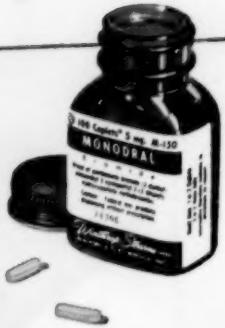

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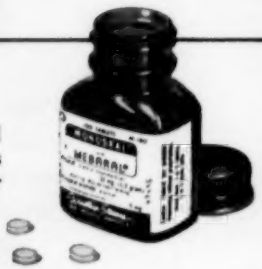

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AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

Vol. 127 SEPTEMBER 1955 No. 9

CONTENTS

EDITORIAL

PROFESSIONAL STANDING, NOT POLITICS

ONE of the most disturbing aspects in the selection of individuals to serve as members of Boards of Pharmacy is that, in some states, the considerations involved are largely—if not solely—political. While it is understandable that, with a change of administration, appointees to a professional board would be selected from those having the political affiliation of the party in power, some little attention surely should be paid to their professional qualifications as well.

Pharmacists are a worldly-wise and mature group of individuals and they know better than to expect perfection when it comes to the conduct of politicians, but it is utterly disgusting when, with hundreds of capable persons to choose from, the appointment to a Board of Pharmacy is made as payment for a political debt and, particularly, when the recipient is not one who has the esteem of pharmacists in the area from which he comes. Such an action is essentially an affront to the citizens of a state and it stamps the appointing governor as one who is not interested in the conduct of professional boards or the welfare of the people whom he was elected to serve.

The duties and obligations of a member of the Board of Pharmacy are such that he must have the unqualified backing of all pharmacists. He must, if he is to live up to his sworn duties, often take actions which may work a hardship on a fellow-pharmacist, but—take them he must—if the public welfare is to be protected and the profession is to be maintained in that inviolate position which is its rightful place. A pharmacist whose background is not that which has gained him universal respect finds it difficult to call other pharmacists to task for violations of lesser importance than some of those he has committed himself in the past. Only a complete villain under such circumstances would take the action indicated under the law and regulations pertaining to it. There is also the lurking and ever-present danger that successful candidates taking the board examination will be those whose political connections are well placed rather than those whose demonstrated knowledge warrants their passing.

One of the tasks which every teacher of pharmacy has is to inculcate in his students not only a respect for the profession, but for the laws governing it and those responsible for their enforcement. When the complexion of the board is such that it does not warrant that respect, the teacher would appear ridiculous were he to attempt to do his duty. Under such circumstances, what, pray, can he do? Is he to completely destroy the idealism of youth and disillusion them about professional integrity and the need for conformity to law? If he does, what will be the eventual outcome? Will, indeed, the public welfare be safeguarded or will he be turning out graduates in pharmacy who believe that connivance, trickery, and dishonesty are the bywords to success?

This is a much more serious matter than it seems on the surface and the body of pharmacy in all of its areas must rise to the occasion when such an event occurs and protest strongly enough to correct the situation. The practice of pharmacy in any state can be no better than the standards set by its Board of Pharmacy. Board membership is a hard and thankless task and one requiring a high sense of public service. There should be no place on a board for political hacks or henchmen and it is up to every pharmacist with the slightest spark of decency to see that this does not happen.

L. F. Tice

THE DAY-DUNLAP 1771 PHARMACEUTICAL CATALOG

By George Griffenhagen *

STEP with me for a minute into a 1771 Philadelphia apothecary shop. Here you will see row upon row of hand-blown flint and black glassware lining the shelves along the walls of the store. Most of the glass bottles are fitted with either ground glass stoppers or "lackered" covers, and all are hand lettered indicating their medicinal contents. You will also see a number of blue and white ointment, syrup, and pill pots which are painted, lettered, and provided with "lackered" covers. A few stoneware jugs and bottles are to be seen, but there are few, if any, of the elegant and richly decorated faience drug jars which were so evident in European pharmacies of the same period.

Such labels as "Cubebae," "Lign. Sassafras," "Rad. Ipecacuan.," and "Cantharides," are prominently displayed on bottles of crude materia medica. There is an abundance of galenical preparations, including such famous items as "Hiera Picra" and "Theriac" and somewhat less famous but equally interesting preparations as "Aq. Mirabilis" (The Wonderful Water) and "Balsam Universale" (The Universal Balsam). The majority of the formulas for the galenicals can be found in any standard English pharmacopoeia or dispensatory of the period (such as John Quincy's *Pharmacopoeia Officinalis Extemporanea; or a Complete English Dispensatory*, London, 1769). Antimony and mercurial preparations, such as calomel or "antimonium cath." (purging antimony) are numerous; and items so characteristic of medieval pharmacy as "axungia viper" (viper's fat) or "chelae cancr" (crabs' claws) can be purchased.

Patent medicines are few but very popular. Among the most widely sold in 1771 were Anderson's pills, Bateman's drops, British oil, Daffy's elixir, Godfrey's cordial, Hooper's pills, James's fever powders, Lockeyr's pills, Stoughton's elixir, and Turlington's balsam.

Drug sundries which can be purchased in the 1771 apothecary shop includes tooth brushes and boxes of tooth powder, nipple shells (for the nursing infant), urinals, "glyster" (enema) pipes, surgical

* Acting Curator, Division of Medicine and Health, Smithsonian Institution, Washington 25, D. C.

dressings (tow and lint), and a variety of cologne for the ladies (such as Lavender water, Hungary water and Eau de Carmes). All types of surgical instruments were offered for sale by the 1771 apothecary, including those for amputation, trepanning, dentistry, and bloodletting.

For compounding prescriptions, the apothecary employed a variety of utensils. At least several types of mortars and pestles were kept on hand, including those made of flint glass, marble, iron, and brass. For powdering, a fine Cypress sieve was employed. Scales either took the form of the large brass counter balance for bulk weighing, or the small boxed pocket scale, with Apothecary's grain weights. Bolus knives and spatulas were used for rolling pills on Delftware pill tiles, and gold or silver leaf was kept on hand for gilding or silvering the pills when desired. Glass flint funnels and filtering paper were available for liquid preparations.

For dispensing, the common green corked vial was most commonly employed, but more expensive flint vials were available when desired. Pills, and other solid preparations, were commonly dispensed in pill boxes made from specially prepared "papers."

An important business of the 1771 apothecary was the sale and refitting of medicine chests which were commonly employed for shipping, plantations and iron-works. As the sale of a medicine chest was generally a sizable purchase, special attention was given this end of the business.

The finances of the apothecary were handled far more leisurely than today. At least one 1771 Philadelphia druggist gave regular customers a 15 percent discount on all purchases if they were paid within six months; 7½ percent discount was allowed for payments between six and nine months, but interest was expected on all debts over a year's standing.

This brief, but interesting, picture of a 1771 American drugstore has been taken in its entirety from a recently discovered pharmaceutical catalog which was published by John Dunlap of Philadelphia in the year 1771.

John Dunlap was one of the leading printers in the city at that time. He was born in the north of Ireland in 1747, and came to this country to apprentice to his uncle, William Dunlap, a Philadelphia printer. John Dunlap succeeded his uncle's business in 1766, and expanded the business in 1771 to include "many pieces of job printing," including a pharmaceutical catalog and a newspaper entitled

the *Pennsylvania Packet and General Advertiser* which eventually became the first daily newspaper to be published successfully in this country (1-3).

Three copies of Dunlap's 1771 pharmaceutical catalog have thus far been located, one in the Rare Book Room at the Library of Congress, Washington, D. C., and two copies in the Library of the American Philosophical Society, Philadelphia, Pa.

The catalog proper is composed of twenty-nine pages. 793 drugs are listed on the first twenty-three pages under the heading "Catalogus Medicinarum." Two pages of "Shop Furniture," one page of "Patent Medicines," one page of "Surgeon's Instruments," one page entitled "Hill's Medicines," and a page of "Additional Articles" complete the catalog.

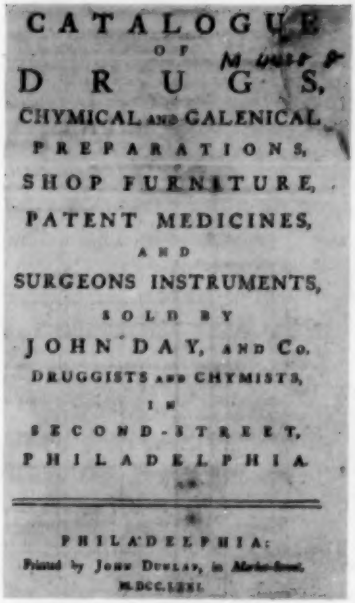
The Dunlap catalog merely enumerates the articles, leaving four columns headed "pound," "4 ounces," "1 ounce," and "1 dram," for the prices and/or quantity to be inserted by the druggist. According to Kremers and Urdang, (4) this was the custom for all early American catalogs prior to 1820's, because the economic and trade situation at that time was not sufficiently stabilized to make fixed prices workable.

One of the two catalogs preserved at the Library of the American Philosophical Society is entitled as follows:

CATALOGUE OF DRUGS, CHYMICAL AND GALENICAL PREPARATIONS, SHOP FURNITURE, PATENT MEDICINES, AND SURGEONS INSTRUMENTS, SOLD BY JOHN DAY AND CO. DRUGGISTS AND CHYMISTS, IN SECOND-STREET, PHILADELPHIA—PHILADELPHIA: Printed by JOHN DUNLAP, in Market-Street. M.DCC.LXXI.

The second page of the John Day Catalogue contains the following foreword: "The Drugs are engaged of the very first Quality, the Chymical and Galenical Medicines are warrented and faithfully prepared by JOHN DAY. Purchasers to the Amount of Twenty Pounds, or upwards, on paying immediate Cash shall be allowed 15 per Cent Discount; constant customers will be allowed the same Abatement for Payments made within six months from the Time of Purchasing; also 7 1-half per Cent. for Payments between the sixth and ninth Month; No Discount will be allowed after that Time, and Interest is expected for all Debts of above a Year's standing."

The penned additions on this catalog appear to be an inventory or an order rather than prices.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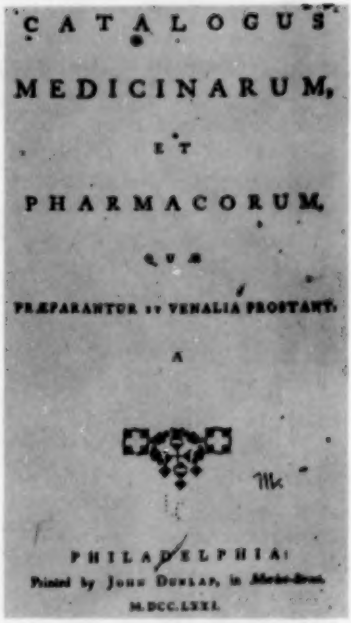
John Day *Catalogue of Drugs* published by John Dunlap of Philadelphia in 1771. Photograph courtesy of the Library of the American Philosophical Society, Philadelphia, Pa.


CATALOGUS
MEDICINARUM,
ET
PHARMACORUM,
QUÆ
PRÆPARANTUR ET VENALIA PROSTANT,
A
PHILADELPHIA:
Printed by JOHN DUNLAP, in Market-Street.
M.DCC.LXXI.

Catalogus Medicinarum, et Pharmacorum, published by John Dunlap of Philadelphia in 1771. Photograph courtesy of the Library of Congress, Washington, D.C.


Price Book
June 4th 1790

Catalogue published by John Dunlap of Philadelphia and bound in blue covers inscribed "Price Book, June 4th 1790." Photograph courtesy of the Library of the American Philosophical Society, Philadelphia, Pa.

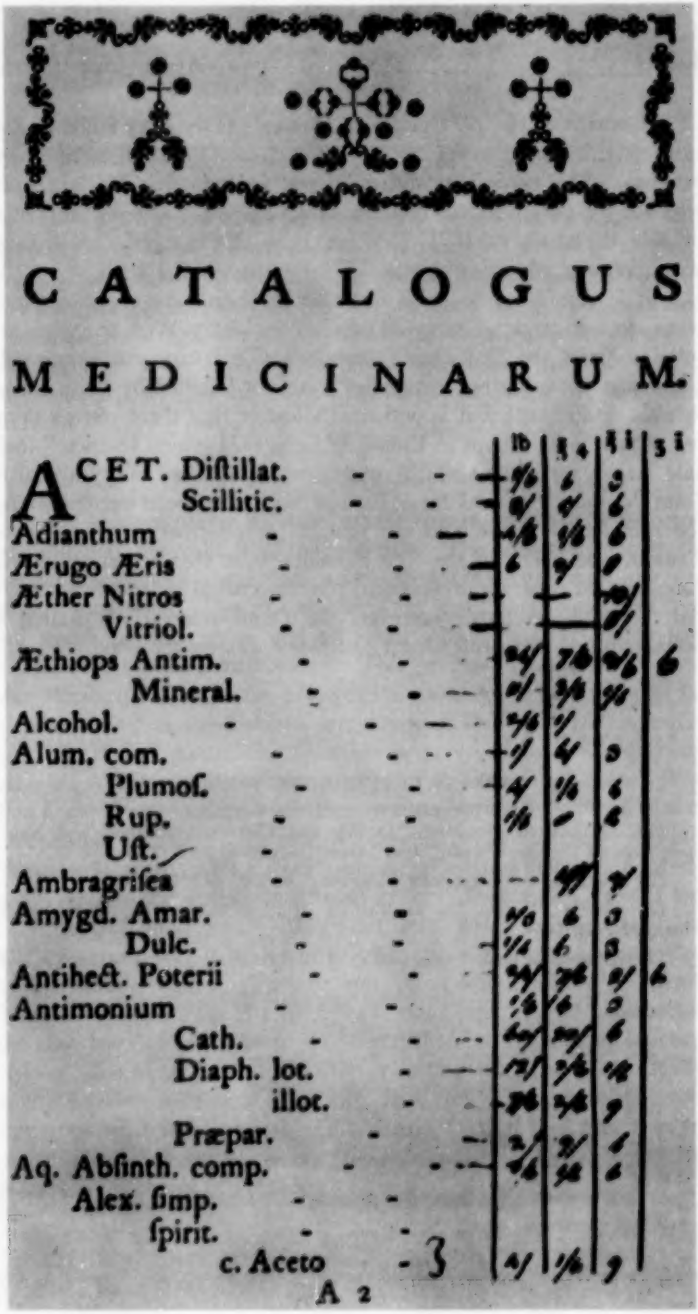
The copy of the Dunlap catalog preserved in the Library of Congress is entitled: CATALOGUS MEDICINARUM ET PHARMACORUM QUAE PRAEPARANTUS ET VENALIA PROSTANT A—(CATALOG OF MEDICINE AND DRUGS WHICH ARE PREPARED AND OFFERED FOR SALE BY——)* PHILADELPHIA: Printed by JOHN DUNLAP, in Market-Street. M.DCC.LXXI. The area which is apparently intended to be inscribed with the name of the distributing druggist is left blank in this copy. Except for the title page, and the elimination of the foreword, the catalog is identical with the John Day Catalog, save the penned insertions. The penned prices start on the first page and end abruptly on page 18; no prices appear in the remainder of the catalog.

The third copy has no separate title page or foreword. The catalog is instead bound in a blue cardboard cover, and the front is inscribed in ink: "Price Book June 4th, 1790." Inside of the front cover is the penned inscription: "J. Henry, 1790"; and on the last page following the announcement of the availability of medicine chests appears the penned inscription: "by Jackson & Smith, Philadel. Second Street." The name "Dr. Tully R. Wise, Eastern Shore of Virginia" appears on the back cover. The penned prices are substantially the same as they appear in the Library of Congress copy, except that they appear scattered throughout the entire catalog.

Apparently the same catalog as published by John Day, was also made available for other apothecaries of the city, either by Day or by Dunlap. Each druggist was to inscribe his own name in the appropriate place on the cover. It is not known, however, whether it was John Day who ordered these unidentified catalogs from Dunlap for distribution, or whether it was John Dunlap who seized upon the idea to sell unidentified catalogs to other apothecaries of the city. Perhaps John Day was using this novel device to compete with the wholesale firm of Christopher Marshall, then the largest in the city.

These catalogs were obviously used for a number of years. Even following the Revolutionary War, (1790) copies were still available (either directly from Dunlap who was still in business, or from the original stock owned by Day). In the case of the 1790 copy, the original title page was undoubtedly removed and the catalog section was bound in a plain blue cover.

* Dr. George Urdang suggests that a more literary translation would be "Catalog of Medicines and Drugs of which Preparations and Salable Forms can be Purchased at. . . ."



CATALOGUS

MEDICINARUM.

	lb	℥ 4	℥ i	ʒ i
ACET. Diſtillat.	5/6	6	2	
Scillitic.	6/	4/	6	
Adianthum	4/8	1/8	6	
Ærugo Æris	6	2/	0	
Æther Nitros			2/	
Vitriol.			0/	
Æthiops Antim.	2/	7/6	2/6	6
Mineral.	0/	3/8	2/	
Alcohol.	2/6	1/		
Alum. com.	1/	4/	2	
Plumoſ.	4/	1/6	6	
Rup.	1/6	—	6	
Uſt.				
Ambragriſea	—	—	3/	3/
Amygd. Amar.	5/0	6	2	
Dulc.	1/4	6	2	
Antihect. Poterii	3/	3/6	2/	6
Antimonium	1/6	6	2	
Cath.	4/	2/	6	
Diaph. lot.	12/	3/6	1/6	
illot.	3/6	3/6	9	
Præpar.	2/	2/	6	
Aq. Abſinth. comp.	5/6	3/6	6	
Alex. ſimp.				
ſpirit.				
c. Aceto	4/	1/6	9	

A 2

First page of John Dunlap's *Catalogus Medicinarum* showing penned prices for the pharmaceuticals listed. Photograph courtesy of the Library of Congress, Washington, D.C.

A search of the 1771 issues of Dunlap's newspaper failed to disclose any information as to the production or distribution of the catalogs. The newspaper did, however, indicate that Day's project was not the only business relation which Dunlap had with the Philadelphia druggists in 1771. Robert Bass, Philadelphia apothecary, was a regular advertiser in the 1771 *Pennsylvania Packet.*

It is significant to point out that the hardware supplies which were stock-in-trade of many of pre-Revolutionary War druggists are missing from the Day-Dunlap catalog. This may not necessarily mean that these hardware supplies were not handled by these Philadelphia druggists, but it is perhaps indicative that there were a number of apothecary shops in Philadelphia in 1771 which restricted their sale largely to drugs. This catalog was published six years after John Morgan returned from Europe with the recommendation for the complete separation of the practice of pharmacy and medicine. True, it was not until the Revolutionary War that actual proof was supplied that separate professional pharmaceutical practice was essential for public welfare; however, the Day-Dunlap 1771 catalog is perhaps proof that professional pharmacy was on the way.

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(2) Dictionary of American Biography, vol. v, p. 514, 1930.

(3) Thomas, Isaiah, The History of Printing in America, Joel Munsell, Albany, N. Y., 1874.

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RECENT DEVELOPMENTS IN DIURETICS

THE use of potent diuretics to relieve the edema associated with congestive heart failure has been a standard practice for many years. Such therapy reduces the accumulation of fluid in the body and also reduces the load on the overburdened heart. Organic mercurials are the drugs which have found greatest use as potent diuretics but, recently, some new non-mercurial agents have been introduced for this purpose. In this review, some of this recent work is summarized.

Normal Kidney Function

The kidneys play a most important role in maintaining the composition and the volume of body fluids. The nephron unit is the functioning unit of the kidney and each kidney contains about one million such units. The glomerulus of the nephron unit is a capillary bed which permits water and all small molecules and ions to pass through the capillary membranes. This process is known as glomerular filtration. The plasma proteins are too large to pass through the membrane unless the kidneys are damaged leading to albuminuria.

The rate of glomerular filtration is governed by the hydrostatic pressure within the glomerular capillaries and the rate of blood flow. The filtrate itself is almost identical in composition with blood plasma except that it is devoid of plasma proteins. The rate of glomerular filtration is such that the total volume of extracellular fluid of the body (about 12.5 liters) is filtered every 100 minutes. From this 12.5 liters of filtrate, only 100 ml. of urine reach the bladder. The balance—consisting of water, nutrients, and electrolytes—is resorbed by the kidney tubules. Tubular resorption is a selective process in that those components of extracellular fluid essential for homeostasis are absorbed, while waste products and those substances in oversupply are allowed to pass on into the collecting tubule and, eventually, to the bladder. Tubular resorption is a complex process involving numerous enzyme systems. It also requires the expenditure of energy derived from cellular metabolism—unlike the purely physical process of glomerular filtration.

While tubular resorption is the most important function of the tubules, it is now known that a number of substances are secreted by the tubule. For example, it has been shown that phenol red, para-aminohippuric acid, iodopyracet, and penicillin are secreted into urine by way of the tubule. In addition, it is now established that the tubules can release H^+ and K^+. This—as will be seen—is important in the understanding of the mechanism of action of some of the newer diuretics.

Urine is more concentrated than extracellular fluid and it usually has a lower pH. This acidity results from the release of hydrogen ions (H^+) by the tubular cells which are exchanged for sodium ions (Na^+). These combine with bicarbonate ions (HCO_3^-) in the tubular cells and are returned to extracellular fluid. The source of hydrogen ions in the tubular cells is from the combination of water and carbon dioxide to form carbonic acid; thus,

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-.$$

This reaction is catalyzed by the enzyme, carbonic anhydrase, also present in the tubular cells.

The hydrogen ions exchanged for sodium in the tubular urine combine with bicarbonate ion giving carbonic acid which decomposes into carbon dioxide and water. The carbon dioxide then back diffuses into the tubular cell. When all the bicarbonate in tubular urine has been removed, sodium phosphate (Na_2HPO_4) is converted to sodium biphosphate (NaH_2PO_4) by hydrogen ions exchanged for sodium.

Ammonia can also be formed in tubular cells and released in the tubule where, with H^+, it forms ammonium ion (NH_4^+). This aids in preventing the urine from becoming excessively acid by the resorption of sodium ions exchanged for hydrogen ions by the mechanisms already described.

The net result of these several processes is that bicarbonate ion is conserved for the alkali reserve of extracellular fluid and, yet, the urine at the same time is prevented from dropping too low in its pH. Urine in man has a minimum pH of 4.4-4.5.

Congestive Heart Failure

As a result of reduced flow of blood through the kidney, water and sodium are retained, leading to edema. This places an increased

burden on the heart and may cause it still further loss in efficiency. While Digitalis and related drugs are indicated, certain diuretics to correct edema are very useful and often must be given even though Digitalis therapy is being employed.

The edema seen in congestive heart failure cannot be corrected by reduction of water intake. Actually, a low intake of water may lead to intracellular dehydration, thirst, and oliguria. On the other hand, salt restriction is useful and—provided the sodium intake is restricted—nothing is gained by the reduction in water consumed.

Mercurial Diuretics

Calomel was used as a diuretic by Paracelsus in the sixteenth century. While it has a diuretic effect, it also is a cathartic and it is unpredictable because of its irregular absorption.

Modern organic mercurials are probably the most potent of all diuretics. As much as 10 liters of urine have been known to result in one day from a single injection. Usually, the first injection will cause a loss of water equal to 2.5 per cent of body weight.

The drug Merbaphen (Novasurol) was originally introduced as an antisyphilitic but its diuretic action was soon discovered. This led to the introduction of Mersalyl (Salyrgan) which, in combination with theophylline, is still widely employed for its diuretic effect. Many other organic mercurials have been developed, all having a similar pharmacologic action.

Organic mercurial diuretics act in the form of $R\text{-}Hg^{+}$. They are rapidly taken up and excreted by the kidney. Thus, Neohydrin labeled with Hg^{203} has been shown to be present in the kidney 6 hours after administration in concentrations 500 times that in the plasma.

It is presently believed that mercurial diuretics act by the inhibition of SH-activated enzyme systems essential for renal tubular transport. Succinic dehydrogenase is the enzyme believed to be involved. The result is that the tubular resorption of chloride ion (Cl^{-}) is impaired. This causes an increase in the amount of chloride excreted together with fixed cations largely sodium (Na^{+}).

Intensive therapy with mercurial diuretics sometimes causes a systemic alkalosis and such patients may then become refractory to mercury therapy. The administration of ammonium chloride or even hydrochloric acid not only potentiates mercurial diuretics, but also corrects the alkalosis caused by intensive therapy.

The physician has a choice of several excellent organic mercury diuretics. The route of administration usually favored is intramuscular, although some products are available for use intravenously, subcutaneously, orally, and as suppositories. Most of these diuretics are combined with theophylline in order to provide rapid absorption from the injection site and reduce tissue reaction. Thiol diuretics can be administered subcutaneously, which has a certain advantage in that the patient may be trained to administer the drug himself. Products for oral use are usually enterically coated to reduce the likelihood of gastric irritation. The oral route is not always satisfactory because of irregular absorption and interference with normal intestinal function. Suppositories also can be used but, here again, absorption is not entirely predictable and proctitis precludes their use.

Contra-indications

Mercurial diuretics should not be used where there is renal insufficiency or acute nephritis. If the concentrating ability of the kidney is such that a urine with a specific gravity of at least 1.015 is formed, it is generally considered safe to use them.

The intravenous administration of mercurial diuretics to persons hypersensitive to mercury has been known to cause rapid death. Even when administering the drug intramuscularly, it is best to give a small test dose. A patient sensitive to one drug may tolerate another quite well.

Mercury poisoning is rare except in patients with renal insufficiency or after very prolonged use. In such cases, Dimercaprol has proven useful in eliminating mercury from the tissues.

Sulfonamide Diuretics

In 1949, Schwartz demonstrated that sulfanilamide in large doses had some effect as a diuretic in congestive heart failure. It was later shown that sulfanilamide inhibited the enzyme carbonic anhydrase and produced disturbances in the acid-base balance of the body.

Roblin and his associates then synthesized a large number of sulfonamide derivatives in an effort to find an even more potent carbonic anhydrase than sulfanilamide. A number of heterocyclic sulfonamides were found to possess this effect. It was also found that substitution on the sulfonamide nitrogen destroyed the activity

of the compound as a carbonic anhydrase inhibitor. This explains why most sulfonamides used therapeutically as anti-infectives do not inhibit carbonic anhydrase.

One of the most useful compounds in this category is Acetazoleamide (Diamox-Lederle). Chemically, this is 2-acetylamino-1, 3, 4-thiadiazone-5-sulfonamide.

This compound has been shown to inhibit carbonic anhydrase *in vitro* in a concentration of only 1.4 mcg./L. In the kidney, the inhibition of carbonic anhydrase depresses the rate of carbonic acid formed and, therefore, the amount of hydrogen ion available for exchange for sodium in tubular urine. The result is a reduction in the resorption of bicarbonate, the urine becoming neutral or even alkaline and a systematic acidosis develops. At the same time that sodium and bicarbonate ions are excreted in the urine, large amounts of water pass with them reducing edema.

Intermittent Therapy

If the drug is given continuously, a mild acidosis results and diuresis soon stops as conservation of bicarbonate ensues. If only a single daily dose is given, the effect lasts only a few hours and renal compensation for the disturbance in acid-base balance can take place. As a result, the next dose produces another diuresis.

If Diamox is given to patients without edema, little or no diuresis results after the first day, since compensatory mechanisms come into play. In edema, the drug will continue to cause loss of extracellular fluid until normal weight is obtained.

Combination with Organic Mercurials

Since the mercurials cause loss of chloride ion together with sodium, and Diamox causes loss of bicarbonate with sodium, their combination in therapy is considered very useful. Mercurials produce a systemic alkalosis and Diamox, a systemic acidosis. Their combined use tends to offset each other's action in upsetting the acid-base balance of the body.

When used together, they should be used on alternate days or else Diamox used and only an occasional dose of the mercurial given as a supplement.

Dosage

Diamox is supplied as 250 mg. tablets and in ampuls containing 500 mg. The dose is 250-500 mg. once daily or every other day. At least eight hours should intervene between doses. Acidifying salts, such as ammonium chloride, rather than potentiating the diuretic effect as is the case with mercurials, interfere with the diuretic action.

The drug does not increase diuresis if the dose is increased. It is contra-indicated in metabolic acidosis, in patients with a previous Na^+ and K^+ loss and in Addison's disease.

Diamox seems most useful in preventing edema in cardiac patients and it also can greatly reduce the frequency of mercurial injections required.

Other Applications

The known value of ketogenic diets in epilepsy has led to the use of Diamox in this disease, particularly in cases refractory to other anti-epileptic drugs. There is some evidence that Diamox may be useful in hyperkaliemia such as following surgery, diarrhea, or high potassium intake.

The most surprising application has been in glaucoma where the drug has been shown to reduce dramatically the intra-ocular pressure. This is accomplished by a suppression of inflow of aqueous humor into the eye. This effect continues even after a patient becomes refractory to Diamox diuresis. A second sulfonamide diuretic (Dirnate —Sharp & Dohme) is under clinical study. This chemically is para-sulfamidobenzoic acid.

Aminometramide

Another non-mercurial diuretic is the drug aminometramide (Mictine—Searle). Chemically, Mictine is an aminouracil; its name is 1-allyl-3-ethyl-6-aminotetrahydropyrimidinedione.

The mechanism of action of Mictine is not precisely known except that it interferes with the tubular resorption of sodium—probably by a blocking action on its transport mechanism. Mictine seems most useful in maintaining the patient edema-free, although in severe edema mercurial diuretics may first be needed to bring the patient under control.

Mictine is supplied in 200 mg. tablets. The dose in severe edema is 4-6 tablets daily with meals for initial diuresis and, then, 4 tablets daily. In less severe cases, the initial doses should be only 4 tablets daily. The drug is prescribed on an interrupted schedule. It is taken on alternate days or on each of three consecutive days followed by its omission for the next four days.

The only side effects so far reported are some instances of gastrointestinal disturbances such as anorexia or nausea.

In summary, it may be said that the newer non-mercurial diuretics offer interesting and useful therapeutic opportunities. While not as powerful as the organic mercury compounds, they do act by a different mechanism and can be used successfully in many cases.

CLINICAL STUDIES ON ANTICANCER AGENTS. VII.

By John R. Sampey *

* Professor of Chemistry, Furman University, Greenville, S. C.

THIS paper brings the number of articles surveyed on current clinical applications of anticancer agents to more than 850 (163). In this installment it will be noted that 6-mercaptopurine and nitrogen mustards have been used most extensively against leukemia and allied diseases, while the sex hormones, cortisone and ACTH have been employed against a wide spectrum of neoplasms. Investigations with radiophosphorus and radiogold lead in the rapidly expanding field of radioisotopes. The search for clinical applications of new anticancer agents is reflected in the more than 30 reports under miscellaneous agents.

I. Inorganic Chemicals

Radiophosphorus. Huguenin and associates (97) reported clinical remissions in patients with Hodgkin's disease following P^{32} therapy. Lawrence (113) has described the control of polycythemia in 172 patients with radiophosphorus, and Lehrner (114) and Croizat, et al. (43), reported less extensive trials with the isotope on polycythemia. P^{32} therapy has proved effective against melanomata, (126), lung carcinoma (156) and mycosis fungoides (129). Radioactive chromic phosphate ($CrP^{32}O_4$) has been employed successfully against cancer of the prostate and bladder (133), and breast cancer (142, 157).

Radiogold. Au_1^{198} has been used to control malignant effusions (41, 86, 110, 114, 167, 191, 193). It has also produced clinical improvement in patients with leukemia (5), cancer of the prostate 63), and ovary, uterus, neck, etc. (91, 131, 154, 193).

Radioiodine. I^{131} therapy has been explored by a number of investigators (25, 66, 114, 171, 172). Kory, et al. (112), found I^{131} totally ineffective in patients with metastatic malignant melanoma.

Radiocobalt. Del Buono (51) preferred Co^{60} to roentgen and radium therapy. Lehrner (114), and Bessler (21) included Co^{60} in their treatment of carcinomas.

Radioyttrium. Y^{90} has proved effective in malignant effusions (6, 174).

Radioarsenic. As^{76} was employed against lymphomas (125).

Zinc. Brohult (33) induced clinical improvement in acute leukemia with metal binding β-globulin with zinc metal.

$Fe_3(OH)_8$ Schotten (166) reported good results with one patient with carcinoma of the rectum, and two with breast cancer, following injections of $Fe_3(OH)_8$.

II. Organic Nitrogen Compounds

6-Mercaptopurine. In a series of papers before the New York Academy of Sciences on April 30-May 1, 1954 on leukemia and allied neoplasms it was shown that 6-MP was one of the most effective drugs in the treatment of these diseases (18, 23, 35, 37, 46, 52, 54, 59, 65, 69, 82, 83, 93, 100, 104, 118, 143, 145, 146, 153, 155, 159, 164, 179, 195). Hall, et al. (83), reported 60% remissions in leukemic patients treated with 6-MP alone or in combination with 6-thioguanine and azaserine.

Nitrogen Mustards. Nitrogen mustards have been employed in the therapy of Hodgkin's disease (1, 22, 96, 125, 185, 188, 196), leukemia (185), lung neoplasms (14, 44), skin cancer (75, 96), lymphomas (158), polycythemia (175), granuloma (121), and cancer of the esophagus (147). Nitromin caused remissions in chloroma (85). Bonner, et al. (30), noted improvement in patients with inoperable carcinomas after nitrogen mustard therapy.

TEM. Triethylene melamine has proved one of the most useful drugs in the treatment of leukemia (12, 13, 29, 84, 117, 144, 158, 190, 196), Hodgkin's disease (13, 56, 84, 117, 190, 196), and lyphomas (12, 13, 61, 62, 144, 190). It has also been successful in the management of ovarian carcinoma (180), lung carcinoma (190) and gastric neoplasms (117).

Urethan. Urethan has been useful in leukemia (2, 67, 158, 187), multiple myeloma (53) and lymphogranulomatosis (67).

Amines. Chloronaphthylamines have been helpful in the treatment of leukemia (72, 130, 177), Hodgkin's disease (72, 101, 130, 189), mycosis fungoides (72), polycythemia (130), and lung car-

cinoma (177). Marcus, et al. (127), reported these amines were without effect in patients with multiple melanomatosis. Bacq, et al. (8), reduced radiation sickness with β-mercaptoethylamine.

Phosphoramides. Bateman (11) noted objective improvement in patients with breast, ovary and lung carcinomas after TEPA therapy, and Forbes, et al. (64), found this phosphoramide produced improvement in patients with melanomas, Hodgkin's disease and neuroblastoma. TEPA and oxapentamethylene were equally effective in mammary carcinoma therapy (10). OPSPA showed cancericidal activity in patients with advanced malignancies (45).

Thioguanine. This compound induced remissions in leukemic patients (83, 134).

Chloropurine. Patients with leukemia and Hodgkin's disease responded to chloropurine treatment (134).

Sulfapyridine. This drug reduced the leukocytic count in patients with leukemia (24).

Azathymine. This thymine analog produced negative results in cancer patients (58).

III. Folic Acid Antagonists and Analogs.

Aminopterin. This folic acid antagonist induced remissions in leukemic patients (16, 90, 93, 132, 176, 196, 198), and combined with cortisone or 6-MP it proved effective against leukemia (17, 54, 93, 118, 128).

Amethopterin. This antagonist produced remissions in leukemia (90, 164, 198).

Teropterin. This antimetabolite relieved pain in cases of prostatic carcinoma (74), and metastatic masses of the lung and bone (152).

IV. Hormones

Estrogens. Estrogens have been employed in the management of breast cancer (76, 98, 99, 136, 138, 148, 178), and in metastases from breast cancer (3, 15, 42, 105). Estrogen therapy has been combined with castration in the treatment of mammary neoplasms

(38, 48, 59), and also with testosterone and cortisone therapy (173). Female sex hormones have proved effective also in the treatment of prostatic cancer (27, 39, 40, 63, 81, 139, 140, 160, 165 186), multiple myeloma (149), and metastases in chorion-epithelioma (105), Segaloff, et al. (168), reported progesterone was without effect on uterine tumors, while Netter (141) warned of estrogen therapy.

Androgens. Androgens have been employed extensively in mammary cancer therapy (73, 94, 136, 148, 169, 170, 178), including the treatment of a variety of metastases of breast tumors (3, 15, 38, 57, 150). Neoplasms of the prostate also have responded to androgen therapy (68, 139). Seliger (173) used a combination of testosterone, progesterone and cortisone in the management of patients with carcinomas of the prostate, breast and lung. Male sex hormones have been used against dysgerminoma (161) and Hodgkin's disease (32).

Cortisone. Cortisone alone (19, 93, 196), or in combination with aminopterin (17, 54, 128), or 6-MP (164) has proved effective against leukemia. Joint hormone therapy with cortisone and thyroid has been employed for thyroid neoplasms (116). Hodgkin's disease responded to cortisone therapy (56, 122, 124, 125). Marchal (123) has warned of its use with Hodgkin's disease. Prostatic cancer and mammary cancer have responded to cortisone therapy (115, 196).

ACTH. This hormone alone (55, 61, 108, 111, 122), or in combination with 6-MP (93, 118), antibiotics (119), and folic acid antagonists (193) has proved successful with leukemic patients. Hodgkin's disease responded to ACTH therapy (122, 124, 125). Barnard, et al. (9), used a combination of ACTH and terramycin against neoplasms, and Kennedy, et al. (109), employed ACTH in two patients with beryllium granulomatosis. Bridger (31) reported the failure of ACTH treatment in a case of leukemia.

Hydrocortisone and Desoxycorticosterone. Combined endocrine therapy with hydrocortisone and TACE gave 70% survival after 3 years in patients with prostatic carcinoma (40). Broun, et al. (36), employed a combination of desoxycorticosterone, colchicine and ascorbic acid to induce remissions in patients with Hodgkin's disease.

Orchiectomy. The beneficial effect of hormonal imbalance by castration has been investigated in the treatment of mammary cancer (92, 137, 184), prostatic carcinoma (140), and bladder cancer (87).

Hysterectomy. Heckel (88) reported on increased longevity following hysterectomy.

Oophorectomy and Adrenalectomy. Bilateral oophorectomy resulted in complete disappearance of breast cancer in a patient (151). Improvement was noted in women with breast neoplasms, following oophorectomy, adrenalectomy and autotransplantation of grafts of adrenal cortex (20). Flocks (63) used castration and adrenalectomy on patients with prostatic carcinoma, and Whitmore, et al. (194), noted improvement in patients with this neoplasm, after bilateral adrenalectomy. Dargent, et al. (48, 49, 50), reported little benefit from castration and sex hormones in treating breast cancer.

V. Miscellaneous Agents

Antibiotics. Aueromycin, terramycin and chloromycetin with ACTH produced clinical remissions in a number of patients with advanced neoplasms (9, 119). Puromycin also has been used on a variety of neoplasms (197). Aureomycin relieved radiation sickness in patients (7). Heinle (90) employed penicillin, transfusions and folic acid antagonists in the treatment of leukemia. *B. Subtilis* as an antibiotic induced regression in patients with multiple myeloma, leukemia, cancer of the cervix and squamous cell carcinoma (80).

Colchicine. Colchicine has induced remissions in leukemia (77, 106, 107), and Hodgkin's disease (36, 102).

Myleran. 1,4-Dimethanesulfonyloxybutane induced remissions in leukemia (70, 182, 183, 196).

Mefedin and Chloropromazine. A combination of mefedin, fargan and largoetil (60), and chloropromazine plus narcotics (95, 162) have been used to relieve pain in cancer.

Vitamin D_2. Vitamin D_2 produced some response in skin cancer (71).

Polydyn. This agent has been used against cancer of the larynx, lung, breast and ovary (78, 192).

Demecolein. Leukemic patients responded to this alkaloid (26).

Oxapentamethylene. This agent produced clinical improvement in far advanced cases of breast carcinoma (10).

Alkoxyglycerols. These esters reduced radiation sickness (34).

Mustard Gas. Bollinelli, et al. (28), noted good results with 9 cases of Hodgkin's disease.

Chloroacetic Acid. Benign tumors of the buccole cavity responded to trichloroacetic acid (47).

Phenol. Injections of phenol in glycerine or propylene glycol relieved the pain of neoplastic diseases (120).

Polysaccharides. These agents reduced fibrosarcoma in patients (152).

σ-Peltation. This agent induced temporary regression in leukemia and allied neoplasms (79).

Butazolidine. This chemical had similar effect on leukemia (89).

Acinin. Subjective improvement was noted in patients with cancer of the lung, rectum, etc. after the administration of acinin (103).

Nitromin. Striking remissions followed the use of this agent on patients with Hodgkin's disease (135).

Tissue Extracts. Deproteinized aqueous extracts of beef spleen caused regression of skin cancer (4).

Pregnancy. Pregnancy produced a negligible effect on the course of Hodgkin's disease (181).

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SELECTED ABSTRACTS

A Stable Chloramphenicol Collyrium. Fenton, A. H., *Pharm. J. 175:67* (1955). In an attempt to increase the solubility of chloramphenicol in water, it was found that alkaline solutions favored increased concentrations of the antibiotic. At a pH of 8.5 a solution containing 0.3 per cent sodium borate permitted up to 0.85 per cent of chloramphenicol to remain in solution. A mixture of 0.3 per cent sodium borate and 1.5 per cent boric acid having a pH of 7.0 permitted the solution of 0.62 per cent chloramphenicol.

On the basis of these findings a formula was developed which is isotonic, stable for at least 5 months when stored at room temperature, has a pH of 7.0, and is adequately preserved. The formula is as follows:

Chloramphenicol		0.5 Gm.
Sodium Borate		0.3 Gm.
Boric Acid		1.5 Gm.
Solution for Eye Drops (B.P.C.)	to	100.0 ml.

Solution for Eye Drops B.P.C. contains 0.022 per cent methyl-*p*-hydroxybenzoate and 0.011 per cent propyl *p*-hydroxybenzoate in distilled water.

The above formula was also found to withstand cooling to 4° C. without any deposition of crystals.

A Therapeutic Comparison of Oral Iron Compounds. O'Sullivan, D. J., Higgins, P. G., and Wilkinson, J. F., *The Lancet* No. 6888:482 (1955). A group of eighty patients with hypochromic anemia were studied with regard to their response to therapy with oral iron compounds. The compounds employed were ferrous sulfate, ferric hydroxide, ferrous gluconate, and ferrous succinate. All of the compounds were given at the same dosage level, 210 mg. of metallic iron a day divided into three doses. They were given after meals in tablet form and without vitamin supplements. Where achlorhydria was found to exist, hydrochloric acid was administered.

Ferric hydroxide was found to be ineffective in the amount administered. However, the other three iron compounds produced an almost identical average rise in the hemoglobin of the patients treated. The maximal increase in the hemoglobin percentage after 42 days of treatment was 40 per cent with ferrous succinate, 37.5 per cent with ferrous sulfate, and 31.1 per cent with ferrous gluconate.

A few patients were intolerant, exhibiting nausea and vomiting, to one of the oral compounds but in no case were they intolerant to all three of the effective compounds. Thirteen per cent were intolerant to ferrous sulfate and 4 per cent each to ferrous gluconate and ferrous succinate. There were seven patients, not included in the study, that were completely refractory to all four compounds orally. However, they responded to intravenous iron therapy.

When these compounds were compared on a cost basis it was found that ferrous sulfate was much less expensive than either of the organic iron preparations. Therefore, in view of the excellent and essentially equal response obtained with ferrous sulfate, the authors concluded that ferrous sulfate is the oral iron compound of choice. One of the other organic compounds may be preferred, however, in those patients intolerant to ferrous sulfate.

The Metabolic Effects of Fluorohydrocortisone and of Cortisone in Adrenal Insufficiency. Garrod, O., Nabarro, J. D. N., Pawan, G. L. S., and Walker, G., *The Lancet* No. 6886:367 (1955). Previous reports have indicated that 9-fluorohydrocortisone has an electrolyte effect 180 times that of hydrocortisone in the adrenalectomised dog. The authors compared the effects of fluorohydrocortisone acetate and cortisone acetate in two adults, one with adrenal insufficiency and the other after total adrenalectomy.

It was found that 0.5 mg. of fluorohydrocortisone acetate had a greater sodium-retaining action than 50 mg. of cortisone acetate. The mineralcorticoid activity of the fluoro derivative is, therefore, more than 100 times that of cortisone. It was also found that the glucocorticoid effect of 50 mg. of cortisone acetate was somewhat greater than that of 0.5 mg. of fluorohydrocortisone. Adequate replacement therapy was obtained by combining both steroids with a normal sodium intake.

Chronic Gout Completely Relieved With Salicylate. Marson, F. G. W., *The Lancet* No. 6886:360 (1955). Acute attacks of gout in patients with chronic gout can be controlled when the serum uric acid level is controlled, but this control is usually not achieved until treatment has been continued for several months, according to the author.

A series of 7 cases, taken from a much larger group, were described to show how effective the control of gout can be. The patients received an initial oral dosage of 30 gr. of sodium salicylate three times a day or 0.5 Gm. of probenecid four times a day. The only other therapy was a large liquid intake and colchicine for the acute episodes.

The symptoms of chronic gouty arthritis were relieved in from 2 to 21 months. Acute paroxysms usually ended after the chronic symptoms had ceased, requiring up to 33 months after the start of treatment. However, eventually all painful manifestations of gout were completely relieved. Tophi did not completely disappear in those patients so afflicted.

The serum uric acid level was controlled by means of the above agents. The level required to control the symptoms of the disease varied from patient to patient. A possible explanation of the fact that acute paroxysms occur even with normal uric acid serum levels was given by the author. Urate deposits are absorbed over a long period of time after a normal serum uric acid level is maintained. In areas surrounding tophi, the uric acid level in the tissues is considerably higher than that in the serum. Thus, the author suggested that acute paroxysms of decreasing severity may occur until the urate deposits in tophi are completely absorbed or the residue is insoluble.

Probenecid lowered the serum uric acid levels less than did sodium salicylate and side effects were more common.

Preventive Therapy With Isoniazid Against Experimental Tuberculosis. Palmer, C. E., and Ferebee, S. H., *Pub. Health Rep. 70*:759 (1955). The effectiveness of isoniazid in the prevention of experimental tuberculosis in guinea pigs has been shown. The experimental method involved the use of 1,224 guinea pigs which were divided into 5 groups. The isoniazid was given to 3 groups in their drinking water. It was found that the animals consumed a fairly

constant amount of water so that the dosage could be adjusted reasonably well. The amount of isoniazid taken daily was approximately 25, 5 and 1 milligram per Kg. of body weight in the 3 groups. All of the animals in 4 groups were challenged intraperitoneally with virulent tubercle bacilli. The fifth group acted as a normal control group.

By the end of the tenth week, only 7 per cent of group 4 remained alive. These had been challenged with virulent organisms but had not received isoniazid. Thirty-seven per cent of the animals which had received 1 mg. per Kg. per day of isoniazid were still alive. About 90 per cent of the normal controls and of the groups receiving 5 and 25 mg. per Kg. per day of isoniazid were alive at the end of 10 weeks. After the tenth week the isoniazid was withdrawn. By the 26th week the groups receiving 5 and 25 mg. of isoniazid had still faired as well as the unchallenged normal control group.

At the end of the 14th week selected animals from the groups receiving 5 and 25 mg. of isoniazid were rechallenged. These animals did not die off as rapidly as untreated controls.

The authors concluded that as little as 5 mg. per Kg. per day of isoniazid will protect guinea pigs against a large intraperitoneal challenge of virulent tubercle bacilli. When this dose is given for 10 weeks it will protect the animals from the appearance of the disease after the drug is withdrawn. Resistance to a later virulent infection develops to some extent during the course of an isoniazid-treated challenge. This resistance is at least as great as that produced by BCG vaccination. Whether or not similar results will be obtained in human beings remains to be seen.

The Preparation of Stable Ophthalmic Solutions Containing Physostigmine Salicylate. Ward, K. L., *The Hosp. Pharm. 8:*17 (1955). The author reviewed the literature relative to the preparation of ophthalmic solutions in general and of physostigmine salicylate solution particularly. He then described experimental studies in which the pH of the solution and the antioxidant included were varied.

All of the solutions contained 1 per cent physostigmine salicylate, the containers were the same size and treated alike before filling, two samples were exposed to atmospheric conditions and one was refrig-

erated, and the solutions were assayed as soon as a color change was noticed. The vehicles employed were: water preserved with methyl and propyl para-hydroxybenzoates, a phosphate buffer having a pH of 6.75, and McIlvaine's Buffer (¼ strength) having a pH of 5.0. Sodium sulfite (0.1, 0.2 or 0.5 per cent) or ascorbic acid (0.1 or 0.2 per cent) were employed as the antoxidants. Boric acid (1 or 2 per cent) was included in some of the formulations.

The solution which proved to be the most stable and at the same time essentially isotonic, had the following formula:

Physostigmine Salicylate	1 per cent
Sodium Sulfite, anhyd.	0.1 per cent
McIlvaine's Buffer (¼ strength)	q.s.ad.

The McIlvaine's Buffer had a pH of 5.0 and the following formula:

Solution Citric Acid	0.025 molar	97.0 ml.
Solution Phosphate dibasic	0.05 molar	103.0 ml.

The solution was assayed after 54 days, the solution stored under atmospheric conditions and exposed to light having developed a color change on the 52nd day. The refrigerated sample remained uncolored. The average assay results indicated 92.0 per cent stability of the physostigmine salicylate.

A Potent New Insecticide, DDVP. Quarterman, K. D., *Pub. Health Rep. 70:729* (1955). The potent new insecticide, dimethyl 2, 2-dichlorovinyl phosphate (DDVP), was developed by the laboratory staff of the U. S. Public Health Service's Communicable Disease Center at Savannah, Ga. The compound is not yet available commercially but it is undergoing extensive testing.

DDVP appears to be equally as toxic as parathion to house flies but only one-fifth as toxic to rats as parathion. It has been found to be effective against DDT-resistant house flies by topical application and in poison baits. It will probably be effective in outdoor space sprays for the control of adult flies and mosquitoes and possibly against their larvae. Because of the volatility of DDVP it will probably not be useful as a residual spray and its toxicity will probably make it unsuitable as a spray in occupied buildings.

It is anticipated that DDVP will find its greatest usefulness in the control of agricultural pests now largely controlled with parathion and tetraethylpyrophosphate (TEPP). DDVP appears to be much less toxic than these compounds. It will also leave less residue on food crops than most of the insecticides now in common usage.

The Government has dedicated the discovery of DDVP to the public and any manufacturer may engage in its production in the U. S. without obtaining a license from the Government.

BOOK REVIEWS

Die Chemie der natürlichen Alkaloide (With special reference to their biogenesis). By Gertrud Woker. Ferdinand Enke, Stuttgart, 1953. Paperbound DM78. 448 pages. (Approxim. $19.)

The first part of this monograph deals with the chemistry of alkaloids, their constitution, degradation, and synthesis. Special emphasis is placed upon the biogenesis of these natural products, and is discussed in detail. Thus, the classification of the alkaloids is arranged in accordance with their biogenetic interrelationships. There are three main divisions. The first group deals with compounds constitutionally analogous to glycine-betaine, the formation of these betaines from amino-acids, and the significance of the latter for the genesis of alkaloids in general. The second division comprises alkaloids which are derived from co-dehydrases and their nicotinic acid-amide component. Among others, sparteine, piperine, alkaloids of the betelnut, nicotine, and cinchona alkaloids are discussed.

The last group deals with alkaloids which have a side chain in α-position of the piperidine nucleus. The solanaceous and veratrum alkaloids belong to this division.

The text is supplemented by many literature references which render it very valuable. It is an important addition to the library of any chemist interested in this special field of natural products.

ELSA EHRENSTEIN

British Pharmaceutical Codex, 1954. Published by direction of the Pharmaceutical Society of Great Britain. 1340 pages, including Index. The Pharmaceutical Press, 17 Bloomsbury Square, London. Price: £ 3.3.0d.

The B. P. C. of 1949 was expanded by Supplement, issued in 1952. On the completion of the work of this Supplement, the Codex Revision Committee and its Subcommittees began work on the preparation of the 1954 edition, which was released late last year.

The outstanding importance of the *British Pharmaceutical Codex* as a reference book for physicians and pharmacists is well-known. It also serves an indispensable role in setting drug standards for use in various courts of law under the provisions of the Food and Drugs Act of 1938 (British).

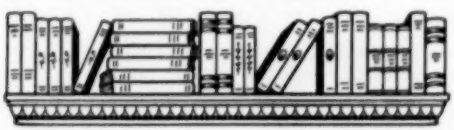
The Codex gives recognition not only to drugs official in the *British Pharmacopoeia* but also to other drugs and preparations either widely used or believed to be of considerable clinical value. The arrangement follows the pattern previously set in that: General monographs comprise Part I; antisera, vaccines, and related substances are included in Part II; preparations of human blood constitute Part III; Part IV is devoted to surgical ligatures and sutures and Part V, to dressings; Part VI is a Formulary giving a large number of pharmaceutical preparations which can be made by the pharmacist since the ingredients are available.

The monographs are similar in style to the 1949 edition except that English names are used as the main title, which is in accordance with standard practices today in both the B. P. and the U. S. P.

A number of appendices are included and a new one dealing with the preparation of isotonic solutions and giving freezing point data is of particular importance to pharmacists.

The *British Pharmaceutical Codex* provides for most pharmacists an even more important reference work than the *British Pharmacopoeia* itself and it is a very useful book even for pharmacists in the United States. A most useful listing, inserted as a separate in the book, is a list of official drugs with their proprietary equivalents. The lack of this is a weakness in our own official books of standards and our British colleagues are to be complemented on the inclusion of such needed reference material.

L. F. Tice



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